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MYCOSIS FUNGOIDES AND SARCOMATOSIS.

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DESPITE the numerous careful studies that have been made of affections of this class during recent years, they are still involved in much obscurity, and their pathology is quite unsettled. It has been found that many cases occur that seem closely related to the known types of mycosis fungoides, but yet vary from these types in some essential particulars, and it may often be embarrassing to decide whether such a case is to be classed as mycosis fungoides, or whether it comes nearer to a true sarcomatosis. Hence Kaposi, who has always maintained that mycosis fungoides is nearly related to the sarcomata, insists that there are transitional forms between mycosis fungoides and true sarcoma, and in the last edition of his work proposes the provisional name "sarcoid tumors" for this whole class of affections, until their pathology has been cleared up and individual types have been more sharply separated. Among his sarcoid tumors Kaposi includes the classical forms of mycosis fungoides, his lymphodermia perniciosa, and the various forms of true sarcomatosis cutis, including the multiple idiopathic pigmented sarcoma described by him.

By far the most able and exhaustive pathological study that has been made of these affections in recent years is that of Paltauf, whose paper on the "Lymphatic Neoplasms of the Skin" was read before the Vienna Congress in 1892. The work is of special value as coming from a skilled general pathologist, than whom no one is more competent to form an intelligent opinion on this subject.

Paltauf reviews the various theories that have been proposed with regard to the etiology of mycosis fungoides, and shows that all are open to grave objections. Histologically the tissue is not like that of the infectious granulomata, and no microörganisms of enduring claim to the title of specific agents have been discovered. The theory of the French that it is a cutaneous lymphoma is disproved by the fact that the round cells that constitute the tumor can be shown in some instances to be derived from the fixed connective-tissue elements, although in certain cases there must be admitted to be a close relationship with leucemia and pseudo-leucemia. Kaposi's theory

that mycosis fungoides is a form of sarcoma, is rejected on the ground that we must cling to the old dictum of Cohnheim that true new formations never disappear spontaneously, as do the tumors of mycosis in a most striking manner. Furthermore, the appearance of the tumors as symptoms in the course of a disease, and the fact that their growth is not centrifugal, are facts opposed to the conception of sarcoma. Paltauf is inclined to include mycosis fungoides in the class of anomalies of vegetation proposed by Kundrat, which comprises pseudo-leucemia and certain forms of lympho-sarcoma. In this sense it is an affection which owes its origin not to a special cause, but to an abnormal reaction of the individual, and depends upon an abnormal vegetation.

However fanciful and vague this theory of Paltauf's may appear to some, it cannot be denied that he has very ably and cogently set forth the reasons against the various theories that had been previously advanced. For a considerable time it seemed highly probable that mycosis fungoides would be finally placed among the infectious granulomata, and several times the demonstration of a specific microbe seemed imminent. The affection is not a common one, and the cases vary so widely that a report of any that diverge from the classical type is of importance. In two cases that happened to come under my notice at the same time, there are many points of similarity with multiple sarcomatosis of the pure type.

Case I.—This patient entered the Massachusetts General Hospital in January, 1890. William G., fifty-two years of age, born in Scotland. Engineer. According to the patient's testimony there was no family history worthy of comment. He had always been a strong, healthy man, and had never had syphilis or other venereal disease. Eight months previously, as he thinks after a strain in lifting, both testicles swelled to twice their normal size, and became hard but not painful. A few weeks after this the cutaneous lesions began to assert themselves, and these consisted of small, soft, red bunches, varying in size from a filbert to a large egg, situated on the thighs, calves, abdomen, chest, arms, and face. During the last eight months he has had a great loss of strength and appetite, and his weight has decreased fifty pounds.

Upon inspection he presented the appearance of considerable cachexia. Scattered over the body were nodules varying in size from a large bean to an egg, firm, rounded, moderately raised above the surface, of a deep bluish-red color. They were movable with the skin and did not seem to extend deeply into the subcutaneous tissues. Some of them showed a central depression. The largest lesion

was on the left side of the upper lip, and the patient said it had existed for three weeks. Some of the tumors were ulcerated slightly, but there were none of the fungous papillomatous appearances seen in the later stages of mycosis fungoides.

Besides these distinctly defined nodules, there were numerous more superficial lesions scattered over the skin, which the patient said had coexisted with the nodules from the outset. These consisted of slightly elevated erythematous and urticarial lesions, pretty sharply bounded from the normal skin, of a reddish-blue color. These areas had often assumed a distinctly annular form from the involution of the center, so that islands of sound tissue had appeared within their boundaries. These erythematous and urticarial lesions were scattered generally over the body, among the nodules and tumors that have been described above. There are also various patches of pigmented skin scattered over the body, which the patient, a most intelligent man, states are the sites of tumors that have existed and subsequently disappeared.

Both testicles were enlarged to twice their normal size, and were hard, smooth, but not painful on pressure. The lymphatic glands were not enlarged.

The patient was immediately treated with subcutaneous injections of liquor potass. arsenitis, three drops daily, in different parts of the body. Under this treatment a number of the nodules, and especially one on the left side of the chin, diminished rapidly in size. A few weeks later, however, he began to complain of severe headache and nausea. There was great prostration, with no physical signs to account for it. There was some pain in the left chest. The temperature was at first normal, but later became high. Finally, great dyspnea and delirium preceded his death.

Autopsy.—Twenty-eight hours *post mortem.* Head not opened. Numerous rounded and flattened elevated tumors in the skin of the trunk and extremities, also one of the lip. Also patches of pale brown discoloration, somewhat indurated. A section through one of these cutaneous nodules showed a homogeneous, reddish-gray new formation of the skin, which proved on microscopical examination to be composed of small, irregularly rounded cells, with a delicate fibrous intercellular substance.

Scrotum. Enlarged to the size of two fists in consequence of a new formation in each testis, resembling that seen in the skin. On the right side the tunica vaginalis was normal, on the left the cavity was obliterated. The epididymis on the right side was the seat of the new formation, being enlarged to the size of the end of the fin-

ger. The left epididymis not increased in size. The new formation extended along each cord to the brim of the pelvis, as elongated ovoid nodules.

Heart and lungs normal.

Spleen increased in size perhaps one-half, firm, dark red. Trabeculæ distinct. Enlargement due to an increase in pulp.

Kidney large. On section pale and moist, with the tubular region distinct. In one kidney a nodule of new formation as large as a pea.

Liver and bladder normal.

Stomach and intestines normal except the vermiform appendix, which was obliterated. In the meso-colon, a short distance above the cecum, was a flattened nodule of new formation as large as a raisin.

Histologically, bits excised from the nodules during life, and material obtained at the autopsy, revealed the same appearances. The lesions consisted of very numerous small round cells, lying within the meshes of a very delicate stroma, which they had apparently pushed aside. There were occasional small irregular and slightly fusiform cells interspersed, but the round cells predominated. A few vessels could be seen with the cell-growth often thicker along their course. The position of the cell-growth was in the lower layers of the corium, extending upward to the papillary layer. There was, however, in most places, a very narrow layer of sound tissue immediately below the papillæ, and where the cell-growth had not penetrated. The papillæ were everywhere compressed or obliterated. The epidermis was somewhat thinned but otherwise normal. The lesions of the internal organs and of the testicles proved to be of a similar histological character. A careful search was made for microörganisms by the various methods of staining, but none could be found.

In what class is this case to be put? Histologically the lesions were exactly similar to those of mycosis fungoides, with the exception that the papillary layer of the corium was not involved, and that the appearances were less superficial. But the character of the cells and stroma was typical of mycosis fungoides, and presented the variations from true sarcomatosis that have been pointed out by Paltauf and others. The affection of the testicles and the nodules of new formation in the kidney and meso-colon are phenomena that are rare in cases of mycosis fungoides of the pure type, but still they occur.

Clinically the resemblance to true sarcomatosis is quite prominent. The patient's declaration that the testicles had begun to increase in size a little before any cutaneous appearances had asserted

themselves, the absence of the pre-mycosic stage of eczema, and the failure of the tumors to ulcerate and become converted into papillomatous and fungous forms, are facts that point toward true sarcomatosis rather than mycosis fungoides. The short duration of the disease may also be included here. On the other hand, we have to note the disappearance of many of the tumors in the way so characteristic of mycosis fungoides, leaving pigmented areas only to mark their site. Furthermore, the urticarial and erythematous appearances were precisely similar to those described by Bazin in the période lichén oide of mycosis fungoides.

Case II.—At just about the same time (January, 1890) a French Canadian, forty-eight years of age, was admitted to the hospital with a somewhat similar affection, so that the two cases were present at the same time and could be compared. This patient spoke nothing but a French patois which it was very difficult to understand. It was learned that he had never had any venereal disease, that he had been married at the age of twenty, and had four strong and healthy children. Up to eight months ago he had had good general health. At this time he became aware of a swelling of the right nostril, and soon after a broadening of the bridge of the nose, and much redness of this part. There is now a dark red tumefaction of the right ala of the nose, which nearly occludes the nostril. Seven months ago the left testicle began to swell. It is now ovoid in shape, equal in size to the two fists clenched, and not translucent. The next event was six months ago, when a tumor appeared on the R. external malleolus. This tumor is now the size of a hen's egg, elastic, not tender, of a light red color. Five weeks ago he first noticed an eruption, which began on the lower limbs and gradually extended upward. Now both legs from groins to ankles are covered with nodules varying in size from a chestnut to an English walnut. Some of them have a decidedly urticarial appearance; others are of a deep reddish-blue color and suggest vividly, at first glance, erythema nodosum. There is, however, much more infiltration than in the latter affection. The same appearances are seen on the trunk, but not in such numbers. In a few places involution had taken place in the center of the plaques, leaving islands of sound skin surrounded by a ring of infiltration, just as in the first case. There are no lesions upon the head, with the exception of a small growth on the conjunctiva of one eye. The patient complains of no pain from the tumors, but he has lost much flesh and is very weak. According to his account none of the lesions have totally disappeared, although many have lessened in size.

The patient was treated for about two weeks with subcutaneous

injections of arsenic in the form of Fowler's Solution, four minims daily, subsequently increased to six minims. At the end of two weeks he left the hospital somewhat improved. There was a slight diminution in the size of the left testicle, and the obstruction in the right nostril was lessened. The nodules upon the body were slightly less prominent.

Ten days later I saw the patient at his house. He was much weaker. Since the injections of arsenic had been omitted the testicle had increased rapidly in size. The appearances upon the skin were much the same, if anything more pronounced. It was learned that the patient rapidly failed, and died two weeks later without the appearance of any fresh symptoms.

Unfortunately the record of this case is insufficient, as no autopsy was made, and the histological examination is not recorded. It was found, however, to correspond pretty accurately with Case I. The short duration of the disease before the fatal termination—about nine months in one case and eleven months in the other—the implication of the testicles in both cases in the early stages of the disease; the very slight amount of ulceration or breaking down of the tumors; and the presence, in addition to the tumors, of urticarial and erythematous lesions exactly like those that are often seen in mycosis fungoides of the pure type—these are points of similarity that may be especially accentuated.

In one feature, and that an important one, the two cases differ, and that is that so far as could be learned there was no spontaneous involution of any of the tumors in Case II, although there was a considerable improvement under arsenic. For this reason, and because a careful histological examination of the growths is lacking, it may be properly maintained that Case II approaches the type of pure sarcomatosis much more closely than Case I.

Spiegler, in a recent article, relates cases where the histological appearances were precisely those of sarcoma, yet the growths exhibited, contrary to our conception of malignant neoplasms, a circumscribed non-progressive character, and a capacity for complete involution. Hence he would separate these growths from the true sarcomata, as Virchow himself had admitted that the clinical course must be taken into account in the classification of neoplasms.

Are we to keep strictly to the classical conception of sarcoma, as a neoplasm that is incapable of spontaneous involution? If we accept this position Case I cannot be regarded as a sarcoma, and furthermore, the histological character varied from that of sarcoma to some extent. But if we exclude on this ground mycosis fungoides, and

instances like Case I, we must also exclude the multiple idiopathic pigmented sarcoma of Kaposi, one of the attributes of which is spontaneous involution, but which has been accepted as a distinct species of sarcoma, on account of the typical character of its tissue histologically.

It seems to me wisest at the present time to admit that our knowledge of these various affections is in a most confused state, and to keep our minds open to all evidence that may be derived from future studies. It will not do to class mycosis fungoides definitely as an infectious granuloma, as its claim to be placed in that category has not been proved. Many good reasons can be adduced against the theory that it is of a sarcomatous nature; and yet the fact, as I have endeavored to emphasize, that there are cases where it may be difficult to say whether we have to do with mycosis fungoides or sarcomatosis, compel us to admit that a relationship with the sarcomata must still be regarded as a possibility.

With regard to leucemia and pseudo-leucemia, instances of the association of cutaneous tumors with these affections have for a long time been known. It is not my purpose to discuss this subject thoroughly, but to refer briefly in conclusion to two typical cases of pseudo-leucemia, in which nodules, similar to the typical prurigo nodule of Hebra, were found.

Wagner[1] was the first to report three cases of pseudo-leucemia in which nodules were found in the skin resembling those of prurigo, and later Josef[2] has written upon the same subject with the report of a case. The nodules were regarded by Josef as of a leucemic nature, and not as had been assumed by Wagner as of the same nature as true prurigo. This opinion was strengthened by the fact that in the cases of pseudo-leucemia the nodules were found on the head, as well as on the body. Histological details are wanting or meager in both cases.

The two cases that were seen by me at the Massachusetts General Hospital represented typical examples of pseudo-leucemia. In both the glands about the neck were greatly enlarged, in one there was an enormous hypertrophy of these structures. In the first case, a woman of thirty-eight years, there was a light bronzing of the whole skin, that had existed for nine months, and an excessive general pruritus, that was betrayed by numerous excoriations and scratch marks, with considerable eczematous thickening. On the extensor surface of the legs and feet were small, firm nodules resembling, to

[1] *Deutsch. Archiv f. Klin. Med., 38 Bd.*

[2] *Deutsch. Med. Wochensc. 1889, 46.*

a marked degree, the true prurigo nodule, the only difference being that they were somewhat larger, as a rule.

In the second case, also a woman, of about middle age, there was much general cachexia, and a very deep pigmentation of the whole skin, much like that seen in Addison's Disease. There was intense pruritus, and many excoriations from scratching, with some thickening of the skin, or lichenification. Nodules exactly like those of true prurigo were situated on the extensor surfaces of the arms and legs. There were also numerous scars, in some places of considerable size, which were probably the results of violent scratching.

In the first of these cases a nodule was excised from the leg, hardened in alcohol, imbedded in celloidine, and cut into sections, which were stained by the various methods. The results of this examination were interesting. The abnormal appearances in the corium were slight, consisting of a very moderate accumulation of round cells about the blood vessels. The epidermis contained a cyst in the upper portions of the rete Malpighii, the walls of which were formed of cornified epithelium. The contents of this cyst had escaped from many of the sections, but in others it was present as a granular detritus mingled with remnants of blood and epidermal cells. Besides the cornification of the walls of the cyst, the horny layer was generally increased in thickness over the lesion. In short, the appearances were almost precisely similar to those described by Leloir and Kromayer as present in the stage of full development of true Prurigo Hebra, and accorded with the illustrations of prurigo in Leloir and Vidal's histological atlas.

These nodules were regarded by Wagner as analogous to those of prurigo, while Josef seeks to show their variance from the latter type, and to place them in the category of cutaneous lesions of leucemic structure. Despite their occurrence upon the head in one or two instances, it seems to me most rational to regard them as akin to the nodules of true prurigo, as their clinical aspect and histological structure agree completely with the latter. We have also present an intense pruritus, and a pigmentation and thickening of the skin. It is not impossible that a study of cases of pseudo-leucemia which present these prurigo nodules may throw some further light on the much discussed question of Prurigo Hebra. That they do not represent a leucemic neoplasm, but are produced in some way analogous to those of true prurigo, probably through the medium of the nerve channels, seems to me evident.